American Journal of Medical Genetics 63:68–73 (1996)

Osteopathia Striata With Cranial Sclerosis: Variable Expressivity in a Four Generation Pedigree

Rainer König, Christof Dukiet, Andrea Dörries, Bernhard Zabel, and Sigrun Fuchs

Institute of Human Genetics Frankfurt (R.K.,C.D.,S.F.), Children's Hospital at Mainz (B.Z.) and Würzburg (A.D.), Germany

Osteopathia striata is a manifestation of several bone dysplasias. In association with cranial sclerosis it represents a separate entity, which is not limited to the bones but may affect other structures, leading to abnormal face, cleft palate, deafness, heart defects, and vertebral anomalies. Neurological findings range from normal development to marked retardation with hydrocephalus, cranial nerve deficiencies and deafness. Ten families, including our own, clearly demonstrate autosomal dominant inheritance with female preponderance and great inter- and intrafamilial variability. © 1996 Wiley-Liss, Inc.

KEY WORDS: osteopathia striata, cranial sklerosis, macrocephaly

INTRODUCTION

Longitudinal striation of the metaphyses of the long bones was first described by the Dutch radiologist Voorhoeve [1924], who classified this condition as a variant of osteopoikilosis. Fairbank [1925] recognized this bone dysplasia as a different entity and coined the term osteopathia striata. Its occurrence in association with cranial stenosis was noted by Hurt [1953]. Until now at least 34 cases were reported. Most patients represent sporadic cases, although nine published families indicate autosomal dominant inheritance (McK. *166500).

We report here on a new family with six affected individuals in four generations (Fig. 1). Our family and a review of the literature demonstrate that osteopathia striata with cranial sclerosis (OS-CS) is not limited to the bones, as suggested by the name, but that it is a pleiotropic condition with many extraskeletal manifestations.

Received for publication January 2, 1996.

Address reprint requests to Rainer König, Institut für Humangenetik, Theodor-Stern-Kai 7, 60590 Frankfurt/Main, Germany.

Dedicated to Jürgen W. Spranger on the occasion of his 65th birthday with admiration and best wishes.

FAMILY STUDY

Case 1

The proposita (III-2) is the second child of nonconsanguineous parents. After an uneventful pregnancy the child was born spontaneously at term. Birth weight was 4,650 g, length was 51 cm, and occipito-frontal head circumference (OFC) was 38 cm. Heart investigation showed atrial septal defect (ASD) and persistent ductus Botalli (PDB). The ASD closed spontaneously; the PDB was ligated at 2 years. Because of increasing head circumference, pneumencephalography was performed, demonstrating internal hydrocephalus. A ventriculo-peritoneal shunt was implanted. Preoperative roentgenographs of the skull (Fig. 2a) and of the thorax (Fig. 3) showed increased density of the cranial base and striation of the humeral head, ribs, and scapulae, suggesting OS-CS. In addition, the clavicles were long and straight and the dorsal parts of the ribs were widened. A slight scoliosis without bony malformations was noted at 13 years, but required no further treatment. The child attended a normal school. At 14½ years (Fig. 4) she presented the following: length of 166.5 cm (50th–75th centile), weight pg 44.8 kg (25th–50th centile), OFC of 61 cm (>97th centile), prominent forehead, hypertelorism (ICD: 3.7 cm: >97th centile), broad nasal bridge, maxillary hypoplasia, prominent mandible, apparently low-set, posteriorly angulated, "dysplastic" ears. She had slender, long fingers. Pubertal development was normal (Tanner stage 3 for breast and genital development). At the age of 17 years she suffered from right-sided peripheral facial palsy. Despite increasing sclerosis of the cranial base (Fig. 2b), cranial CT scan showed no narrowing of the cranial foramina. The facial palsy disappeared completely within one year. Audiography and visual field examination were normal.

Case 2

The proposita's sister (III-1) had macrocephaly (OFC: 62 cm: >97th centile), relatively flat face, hypertelorism (ICD: 3.6 cm: >97th centile), and broad nasal bridge (Fig. 5). Her psychomotor development was normal; she is working as an engineer. Hearing and visual field examination were normal. Roentgenographs of her skull demonstrated basal sclerosis, and a thickened

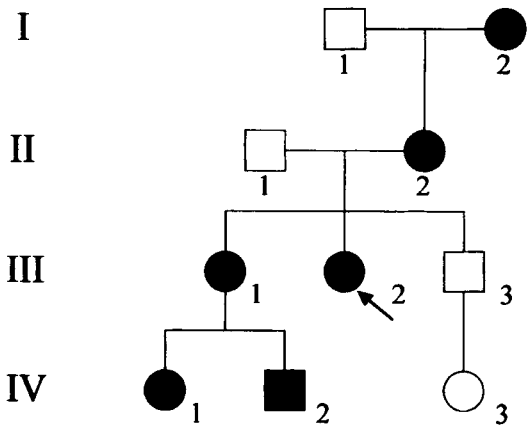

Fig. 1. Pedigree of the family.

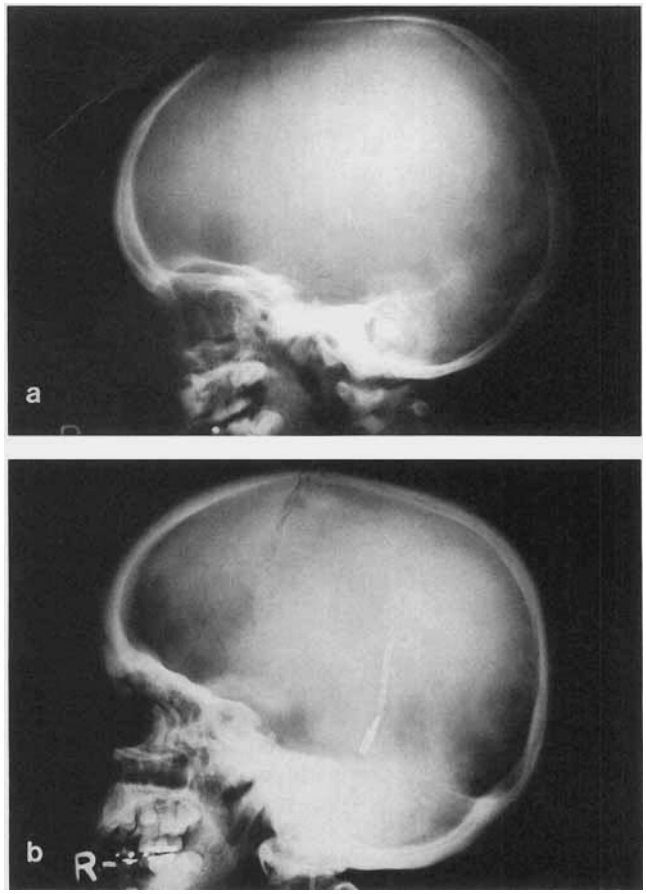

Fig. 2. **a,b:** Lateral skull of the proposita at the age 3 years (preoperative) and 13 years showing increasing density of the cranial base and striation of the ascending ramus of the mandible.

calvaria. Slight striated densities were present in the maxilla and in the ascending ramus of the mandible. Epiphyses and metaphyses of the tibia and femur showed typical linear striated densities (Fig. 6). Faint striations were present in the distal ulna and radius metaphyses. Fan-like striations were seen in the iliac bones together with dense striations in the femoral neck. Vertebral roentgenographs showed spina bifida occulta.

Case 3

The son (IV-2) of case 2 has had normal fetal ultrasound findings at the 18th week of gestation, but at the 32nd week he manifested marked macrocephaly (biparietal diameter: 10 cm) according to the 40th week of gestation. He was born at term. Birth weight was 3,730 g (50th–75th centile), length was 54 cm (75th–90th centile), and OFC was 41 cm (>95th centile). The newborn had a Pierre Robin sequence with submucous cleft palate and bronchoscopically verified tracheomalacia. Cranial CT scan showed ventricular dilatation without signs of increased pressure. In addition, he had flexion contractures of both index fingers and of several toes. He presented severe muscular hypotonia and failure to thrive. At this time, a roentgenogram of the skull was normal. Chromosome analysis showed a normal male karyotype 46, XY. Psychomotor development was retarded. At the age of 2 years he had macrocephaly (56 cm: >95th centile), short stature (75 cm: ≤5th centile) and was underweight (10 kg: ≤5th centile). The face was characterized by prominent, broad forehead, hypertelorism, epicanthus, slight palpebral ptosis, broad, flat nasal bridge, open mouth, thick lips, coarse tongue, small, irregular, malpositioned lower incisors, and retro-micrognathia. He had apparently low-set and posteriorly angulated ears with a prominent anthelix and an overfolded helix (Fig. 7). He had a chronic mucotympanon and audiologic investigations demonstrated left-sided mixed hearing loss. Roentgenographs of the skull showed increased density, particularly in the cranial base and maxilla. Metaphyses of the femur and tibia were dense, but showed no typical striations. The clavicles were abnormally long and straight with broad medial and lateral ends. This clavicular abnormality was also recognizable clinically as protuberances on the shoulder.

Case 4

The daughter (IV-1) of case 2 was born after an uneventful pregnancy by complicated breech presentation. Birth weight was 3,760 g (75th–90th centile), length was 52 cm (75th–90th centile), and OFC was 39 cm (>95th centile). Early psychomotor development was normal, but at the age of 7 years the child showed moderate speech retardation. At the age of 8 1/2 years OFC was 56 cm (>97%). She had a flat face and hypertelorism (ICD: 3.5 cm: >97th centile) (Fig. 8). Hearing and vision were normal. Roentgenographs of the skull showed dense cranial base without striation. Roentgenographs of a tubular bone were not available.

Case 5

The mother (II-2) of the proposita was examined after the diagnosis of OS-CS was made in her daughter. As a child she had had a midline cleft palate, which

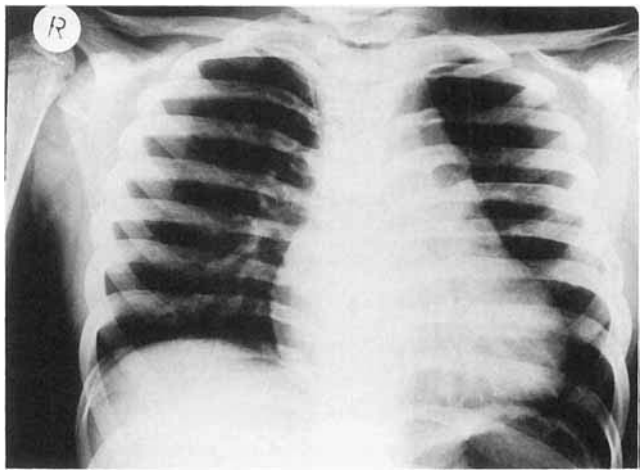

Fig. 3. Frontal roentgenograph of the proposita's chest with dense striation of the humerus, acromion, and ribs, and widening of the dorsal parts of the ribs.

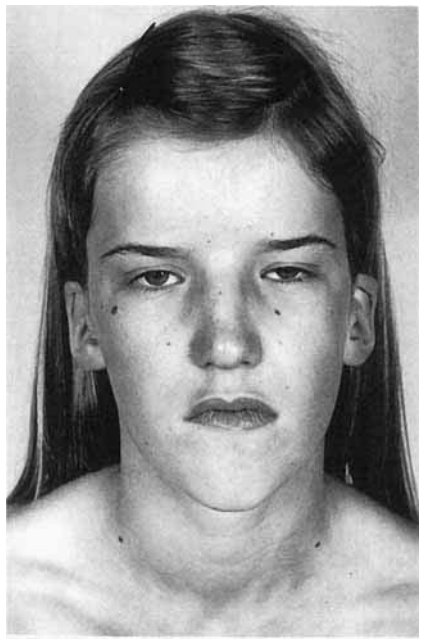

Fig. 4. Proposita at 14 years. Long, flat face with broad nasal bridge and apparently low-set, posteriorly angulated, "dysplastic ears."

was repaired at the age of 4 years. At 27 years a hemodynamically nonsignificant combined mitral valve insufficiency/stenosis was noted. Examination at 54 years showed a slender woman with macrocephaly (OFC: 60 cm: >97th centile), hypertelorism (ICD: 3.5 cm: >97th centile), nasal speech, and pectus excavatum. Roentgenographs showed a dense cranial base with hypoplasia of the left maxillary sinus and fine striation of the femur and tibia. She suffered from mixed hearing loss, requiring hearing aids. Visual fields were normal.

Case 6

The mother (I-2) of case 5 was said to have had a large head and roentgenographs verified the diagnosis of OS-CS.

DISCUSSION

Osteopathia striata usually is a benign roentgenographic finding, observed by chance or in patients complaining of non-characteristic pain in bones and joints. In association with cranial sclerosis, osteopathia striata constitutes a distinct entity which is not limited to the bones but involves various other systems (Table I).

The frequency of roentgenographic signs in OS-CS is demonstrated in Figure 9. The typical and name-giving roentgenographic finding of OS-CS is the fine, uniform, linear striation of the tubular bones, which was seen in all but four patients, particularly in the metaphyses and adjacent diaphyses. Fan-like striations of the iliac bones are present in more than 50% of cases. The ribs may show linear striations parallel to the long axis [Nakamura et al., 1985], increased density with cortical thickening [Paling et al., 1981], wide anterior ends [Winter et al., 1980], or wide dorsal parts (case 1). In our case 3 the clavicles were straight and long with broad medial and lateral ends, causing marked protuberances on the shoulder. Similar clavicular changes were mentioned by others [Gay et al., 1994; Piechowiak et al., 1986; Winter et al., 1980].

Involvement of the skull is manifested by increased thickness and density mostly of the cranial base, but also of the other parts. These roentgenographic findings may be progressive in childhood [Robinow and Unger,

Fig. 5. Patient III-1 at the age of 25 years.

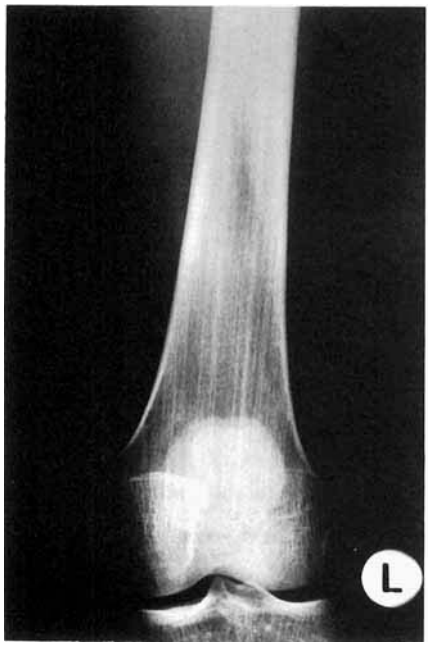

Fig. 6. Frontal radiograph of the distal femur and proximal tibia of patient III-1 with dense linear striations in metaphyseal regions extending into epiphyseal and diaphyseal parts.

Fig. 7. Patient IV-2 at the age of 2 years, showing prominent forehead and posteriorly angulated, "dysplastic" ears. Note protuberances on the shoulder.

1984; Gay et al., 1994; patient III-2], whereas adults have been described without any roentgenographic changes over a period of 12 and 25 years [Franklyn and Wilkinson, 1978; case II-2]. Radionuclide bone scan showed an increased tracer uptake in the skull and tubular bones, suggesting an active metabolic process [Gay et al., 1994; de Keyser et al., 1983].

Cranial CT scan is usually nonspecific. A few authors documented narrowing of the optic foramina [Clementi et al., 1993], hypoplasia of the orbits and middle ear [de Keyser et al., 1983] but in most cases, no narrowing of the cranial nerve foramina was seen [Bass et al., 1980; Gay et al., 1994; Robinow and Unger, 1984; case III-2, case IV-1]. The brain was described as normal [Bass et al., 1980], atrophic [Robinow and Unger, 1984], or hydrocephalic (case III-2). Our proposita is the only one who manifests hydrocephalus, requiring shunting, while all others apparently had macrocephaly without increased intracerebral pressure.

Macrocephaly with frontal bossing, hypertelorism, epicanthic folds, broad and depressed nasal bridge, and flat face give the patients a typical facial impression.

Unilateral peripheral facial palsy and congenital bilateral palsy were reported in three patients. In the case of Kornreich et al. [1988] the palsy subsided within 2 days and within 5 months at a second episode. In our case III-2, the palsy disappeared spontaneously within 1 year. Other cranial nerve deficiencies involved the oculomotor and hypoglossal [Gay et al., 1994], abducens and maxillary (de Keyser et al., 1983], and optic nerves [Clementi et al., 1993]. It was suggested that these cranial nerve deficiencies may be due to narrowing of cranial foramina by the sclerosing process [de Keyser et al., 1983], although only in the case reported by Clementi et al. [1993] cranial CT scan demonstrated narrowing of the optic foramina. In our proposita with palsy of the VII cranial nerve and in the cases of Gay et al. [1994] and de Keyser et al. [1983] no narrowing was seen. So there may be other or additional factors, for example, disruption of nerve-supporting vessels by the sclerosing process, which lead to secondary cranial nerve deficiencies. This hypothesis may explain the transitional character and sponta-

Fig. 8. Patient IV-1 at the age of 8½ years.

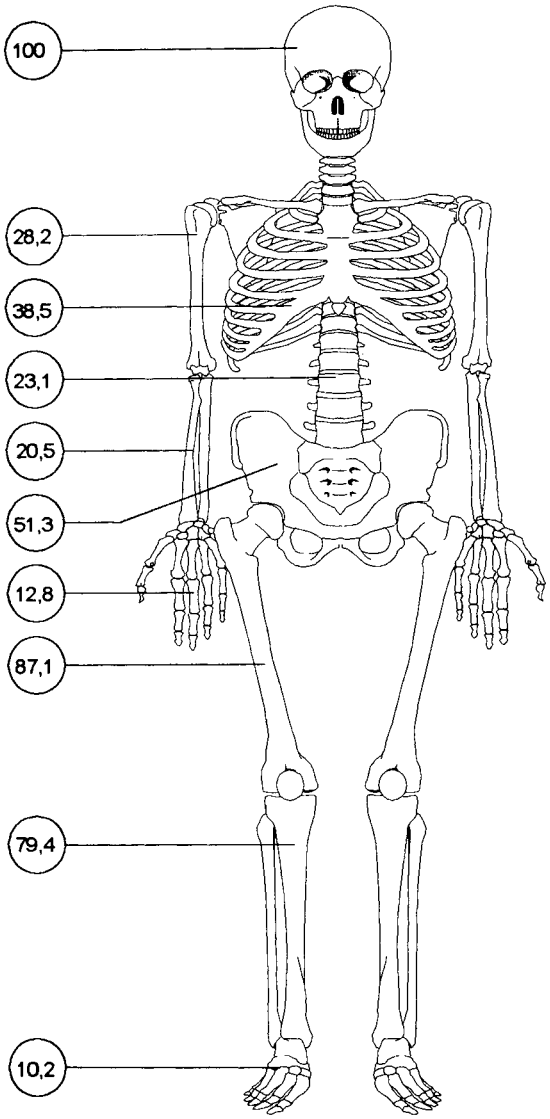

Fig. 9. Frequency of roentgenographic findings in OS-CS (39 patients*).

TABLE. I Clinical Manifestations of OS-CS (39 Patients)*

	%
Macrocephaly	66.6
Frontal bossing	53.8
Broad depressed nasal bridge	53.8
Hearing loss	46.1
Hypertelorism	43.6
Cleft palate	41.0
Hypoplasia of paranasal sinuses	33.3
Sclerosis of mastoids	30.7
Tooth anomalies	30.7
Scoliosis	23.1
Cardiac malformations	20.5
Psychomotor retardation	17.9
Cranial nerve palsies	15.4
Highly arched palate	15.4
Speech delay	10.2

Others:
cataracts, contractures of fingers and toes, delayed bone age, esotropia, headaches, hyperopia, hypospadias, kyphosis, "leonine" face, lordosis, laryngomalacia, pectus excavatum, polydactyly, palpebral ptosis, rib cage abnormalities, short stature, spina bifida occulta, spondylolisthesis, stenotic exteral auditory canals, syndactyly.

*Bass et al., 1980; Bloor, 1954; de Boer and van Gool, 1974; Clément et al., 1982; Clementi et al., 1993; Cortina et al., 1981;Currarino and Friedmann, 1986; Culver and Thumasathit, 1972; Franklyn and Wilkinson, 1978; Gay et al., 1994; Goodmann and Robertson, 1993; Hoeffel and Merle, 1990; Horan and Beighton, 1978; Hurt, 1953; Jones and Mulcahy, 1968; de Keyser et al., 1983; Kornreich et al., 1988; Nakamura et al., 1985; Odrezin and Krasikov, 1993; Paling et al., 1981; Piechowiak et al., 1986; Robinow and Unger, 1984; Sevaux and Galmiche, 1970; Schnyder, 1980; Taybi and Nurock, 1969; Walker, 1969; Winter et al., 1980; own cases II-2, III-1, III-2, IV-1, and IV-2.

neous remission of the palsies due to establishment of collateral vessels.

Hearing deficits were seen in nearly half of the patients. Most cases presented with conductive hearing loss (78.6%). Surgical attempts to mobilize the middle-ear ossicles were unsuccessful because of sclerotic bone thickening and overgrowth from all boundaries of the tympanic cavity [Jones and Mulcahy, 1968; Gay et al., 1994].

Most patients with OS-CS show normal psychomotor development, although about 28% of reported patients presented mild to moderate psychomotor or speech retardation. Despite markedly delayed psychomotor development and hydrocephalus in the first years of life, our proposita attained normal psychomotor development and attended normal school.

Ten familial cases of OS-CS, including male to male transmission, clearly demonstrate autosomal dominant inheritance with quite variable expressivity [Bass et al., 1980; Cortina et al., 1981; Currarino et al., 1986; Horan and Beighton, 1978; de Keyser et al., 1983; Nakamura et al., 1985; Winter et al., 1980; our family]. In general, more female than male patients exhibit a severe phenotype and complications are more common in females than in males. In the present kindred all presumed gene carriers are affected, indicating complete or nearly complete penetrance.

Prenatal diagnosis of OS-CS was first described by Winter et al. [1980]. He reported increased head circumference in a fetus (case 2) at the age of 16 weeks. In another case (case 3) with postnatally verified OS-CS the prenatal ultrasound was normal. Our patient (IV-2) had normal ultrasound findings at the 18th week of gestation and developed macrocephaly in the 32th week of gestation. This agrees with the suggestion of Winter et al. [1980], that only severe cases of OS-CS are recognizable by early prenatal ultrasound study.

ACKNOWLEDGMENTS

We thank Prof. S. W. Bender for his patients' data.

REFERENCES

Bass HN, Weiner JR, Goldman A, Smith LE, Sparkes RS, Crandall BF (1980): Osteopathia striata syndrome: Clinical, genetic and radiologic considerations. Clin Pediatr 19:369–373.

Bloor U (1954): A case of osteopathia striata. J Bone Joint Surg 36B: 261–265.

Boer SM de, van Gool AV (1974): Schedel- en gebitsafwijkingen bij een patiente met osteopathia striata. Ned T Geneesk 118:1373–1380.

Clément A, Garrigues C, Coursault-Durand R, Ledoux-Lebard G, Bonnin A (1982): Une affection osseuse rare, me à ne pas mèconnaitre : L'osteopathie striée. J Radiol 63:673–676.

Clementi M, Bellato S, Rossetti A, Mammi I, Tenconi R (1993): Is visual field reduction a component manifestation of osteopathia striata with cranial sclerosis ? Am J Med Genet 46:724–726.

Cortina H, Vallcanera A, Vidal J (1981): Familial osteopathia striata with cranial condensation. Pediatr Radiol 11:87–90.

Currarino G, Friedmann JM (1986): Severe craniofacial sclerosis with multiple anomalies in a boy and his mother. Pediatr Radiol 16: 441–447.

Culver GJ, Thumasathit C (1972): Osseus changes of osteopathia striata and Pyle's disease occuring in a patient with an 11 year follow-up. Am J Roentgenol 116:640–643.

Fairbank HAT (1925): A case of unilateral affection of the skeleton of unknown origin. Br J Surg 12:594–597.

Franklyn PP, Wilkinson D (1978): Two cases of osteopathia striata, deafness and cranial osteopetrosis. Ann Radiol 21:91–93.

Gay BB, Elsas LJ, Wyly JB, Pasquali M (1994): Osteopathia striata with cranial sclerosis. Pediatr Radiol 24:56–60.

Goodmann JR, Robertson CU (1993): Osteopathia striata: A case report. Int J Paediatr Dent 3:151–156.

Hoeffel JC, Merle M (1990) Osteopathia striata with cranial sclerosis. Roentgenbl 43:465–466.

Horan FT, Beighton PH (1978): Osteopathia striata with cranial sclerosis. An autosomal dominant entity. Clin Genet 13:201–206.

Hurt RL (1953): Osteopathia striata-Voorhoeve's disease: Report of a case presenting the features of osteopathia striata and osteopetrosis. J Bone Joint Surg 35B:89–96.

Jones MD, Mulcahy ND (1968): Osteopathia striata, osteopetrosis and impaired hearing. Arch Otolaryng 87:116–118.

Keyser de J, Bruyland M, Greve de J, Leemans J, Potvlige R, Six R, Ebinger G (1983): Osteopathia striata with cranial sclerosis. Clin Neurol 85:41–48.

Kornreich L, Grunebaum M, Ziv N, Shuper A, Mimouni M (1988): Osteopathia striata, cranial sclerosis with cleft palate and facial nerve palsy. Eur J Pediatr 147:101–103.

McKusick VA (1994): "Mendelian Inheritance in Man," 11th Edition. Baltimore: Johns Hopkins University Press.

Nakamura T, Yokomizo Y, Kanda S, Harada T, Naruse T (1985): Osteopathia striata with cranial sclerosis affecting three family members. Skeletal Radiol 14:267–269.

Odrezin GT, Krasikov N (1993): CT of the temporal bone in a patient with osteopathia striata and cranial sclerosis. Am J Neuroradiol 14:72–75.

Paling MR, Hyde I, Dennis NR (1981): Osteopathia striata with sclerosis and thickening of the skull. Br J Radiol 54:344–348.

Piechowiak H, Goebel FD, Hirche U, Tyrell R (1986): Cranial sclerosis with striated bone disease (Osteopathia Striata). Klin Paediat 198: 418–424.

Robinow M, Unger F (1984): Syndrome of osteopathia striata, macrocephaly, and cranial sclerosis. Am J Dis Child 138:821–823.

Sevaux G, Galmiche P (1970): Sur un cas d'ostéopathie striée. Rev Rhum 3:248–252.

Schnyder PA (1980): Osseous changes of osteopathia striata associated with cranial sclerosis: An autosomal dominant entity. Skeletal Radiol 5:19–22.

Taybi H, Nurock AB (1969): Discussion of osteopathia striata. New York: Alan R. Liss, Inc., for the National Foundation—March of Dimes. BD:OAS V(4):105–108.

Voorhoeve N (1924): L'image radiologique non encore décrite d'une anomalie du squelette: Ses rapports avec la dyschondroplasie et l'osteopathia condensans disseminata. Acta Radiol 3:407–427.

Walker BA (1969): Osteopathia striata with cataracts and deafness. New York: Alan R. Liss, Inc., for The National Foundation—March of Dimes. BD:OAS V(4):295–297.

Winter RM, Crawfurd M, Meire HB, Mitchell N (1980): Osteopathia striata with cranial sclerosis: Highly variable expression within a family including cleft palate in two neonatal cases. Clin Genet 18: 462–474.